Open Access

ISSN: 2663-9491 e-ISSN: 2789-6897

ORIGINAL ARTICLE

Immunohistochemical Expression of HER2/neu in Invasive Ductal Carcinoma of Breast

Raquibul Hasan Kazal[1]*, Sabiha Shabnam[2], Zillur Rahman[3]

Received: 14 October 2026
Accepted: 04 November 2026
Published Online: 15 November 2026

Published by:
Gopalganj Medical College, Gopalganj, Bangladesh

*Corresponding Author

DOI: 10.5281/zenodo.24238431

Copyright © 2026 The Insight

This article is licensed under a Creative Commons Attribution 4.0 International License.s

ABSTRACT

Background: *Globally, breast cancer remains a leading malignancy among women, while in Bangladesh, delayed diagnosis and limited access to specialized biomarker testing continue to challenge optimal management. Among invasive breast cancers, HER2/neu expression is clinically important because it reflects tumor biology and guides HER2-targeted therapy.* ***Aim of the study:*** *This study aimed to determine HER2/neu immunohistochemical expression in invasive ductal carcinoma of the breast and assess its relationship with selected clinicopathological characteristics.* ***Methods & Materials:*** *This cross-sectional observational study included 52 histologically confirmed cases of invasive ductal carcinoma of the breast diagnosed at the Department of Pathology, Chittagong Medical College, and CARE Investigation, Chattogram, using consecutive sampling from March 2018 to February 2020. Formalin-fixed, paraffin-embedded tissue sections were examined histologically and graded, while HER2/neu expression was assessed by immunohistochemistry using a rabbit polyclonal antibody. HER2/neu staining was categorized as negative, weakly positive, or strongly positive. Data were analyzed using SPSS version 26.0, and associations with selected clinicopathological variables were assessed, with $p<0.05$ considered statistically significant.* ***Results:*** *The mean patient age was 48.33 ± 10.81 years (range: 21–73 years), and 98.1% were female. Grade II invasive ductal carcinoma was predominant, accounting for 75.0% of cases, followed by Grade III, 21.2%, and Grade I, 3.8%. Strong HER2/neu expression was observed in 48.1%, weak positivity in 30.8%, and negative expression in 21.2%. No significant association was found between HER2/neu expression and age (p=0.843), estrogen exposure (p=0.116), or tumor grade (p=0.161). Among strongly positive tumors, 80.0% were Grade II.* ***Conclusion:*** *HER2/neu overexpression was common in invasive ductal carcinoma, particularly among Grade II tumors, but showed no significant association with age, estrogen exposure, or tumor grade. Accurate HER2 assessment is therefore important for prognostic evaluation and selecting appropriate targeted therapy.*

Keywords: *Invasive ductal carcinoma, HER2/neu, Immunohistochemistry, Breast cancer, and Histopathological grade*

(The Insight 2026; 9(3): 978-982)

1. *Assistant Professor, Department of Pathology, Sir Salimullah Medical College, Dhaka, Bangladesh (ORCID: 0009-0002-7133-3067)*
2. *Assistant Professor, Department of Pathology, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh*
3. *Professor, Department of Pathology, Bangladesh Medical University, Dhaka, Bangladesh*

INTRODUCTION

Globally, breast cancer remains one of the most important malignancies affecting women and continues to impose a substantial burden on health systems. According to GLOBOCAN 2022 estimates, approximately 2.3 million new female breast cancer cases and 666,000 related deaths occurred worldwide, accounting for 11.6% of all newly diagnosed cancers and 6.9% of cancer deaths [1]. Over recent decades, incidence has increased across most geographical regions and age groups, with particularly important implications for countries undergoing demographic and socioeconomic transition [2]. Across Asian populations, considerable heterogeneity has also been observed in age at presentation, tumor phenotype, stage, receptor profile, and survival outcomes [3]. Within Bangladesh, breast cancer represents an increasingly important public health concern, where limited awareness, delayed detection, inadequate screening opportunities, and restricted access to specialized diagnostic services may contribute to unfavorable outcomes [4]. Based on recent estimates reported in Bangladeshi research, approximately 12,904 new breast cancer cases and 6,783 deaths occurred nationally in 2020, with the burden projected to increase substantially in coming decades [5]. Within South Asian populations, relatively younger age at diagnosis and considerable biological heterogeneity further emphasize the need for appropriate pathological and molecular characterization [3,6]. Among invasive breast malignancies, invasive ductal carcinoma constitutes the predominant histological type. Beyond conventional histopathological classification and grading, assessment of predictive biomarkers has become essential for therapeutic decision-making. In particular, human epidermal growth factor receptor 2 (HER2/neu), encoded by the ERBB2 gene, is a transmembrane receptor tyrosine kinase whose amplification or overexpression drives cellular proliferation, survival, invasion, and tumor progression [7,8]. Clinically, HER2-positive breast cancer historically demonstrated aggressive behavior; however, outcomes have improved markedly following the development of HER2-targeted therapies, including

ISSN: 2663-9491 e-ISSN: 2789-6897

trastuzumab, pertuzumab, tyrosine kinase inhibitors, and antibody-drug conjugates [9,10]. For routine pathological assessment, immunohistochemistry remains a practical and comparatively accessible method for evaluating HER2 protein expression, particularly in resource-limited settings. Nevertheless, accurate interpretation is crucial because equivocal immunohistochemical findings may require confirmation by in situ hybridization, and differences in fixation, laboratory techniques, scoring, and interpretation can influence reported HER2 status [11,12]. More recently, recognition of HER2-low breast cancer has further increased the clinical importance of distinguishing HER2 expression levels because selected tumors without conventional HER2 amplification may also benefit from newer antibody-drug conjugates [8]. Despite these advances, substantial geographical variability persists in reported HER2 positivity. In a large South Indian series, HER2 positivity was approximately 15% while studies from neighboring Asian populations have shown different distributions and clinicopathological associations [3,6,7]. Such variation may reflect differences in population characteristics, tumor biology, laboratory methods, sampling, and interpretation. Consequently, locally generated evidence remains important, particularly where contemporary data regarding HER2/neu expression in invasive ductal carcinoma are limited. Therefore, this study aimed to determine HER2/neu immunohistochemical expression in invasive ductal carcinoma of the breast and evaluate its relationship with selected clinicopathological characteristics.

METHODS & MATERIALS

This cross-sectional observational study was conducted among patients diagnosed with invasive ductal carcinoma of the breast at the Department of Pathology, Chittagong Medical College, Chattogram, and CARE Investigation, Chattogram. The study included 52 histologically confirmed cases of invasive ductal carcinoma from March 2018 to February 2020. Cases with adequate clinical information and sufficient paraffin-embedded tumor tissue for immunohistochemical evaluation were considered eligible. Cases with inadequate tissue, extensive necrosis, or incomplete clinicopathological information were excluded. Patients were enrolled using Consecutive sampling. Relevant demographic and clinical information, including age, sex, history of estrogen exposure, and other available risk-factor information, was obtained from clinical records and recorded using a structured data collection sheet. Histopathological diagnosis and grading of invasive ductal carcinoma were performed on hematoxylin and eosin-stained tissue sections according to the institutional diagnostic criteria used during the study period. Tumors were categorized as Grade I, Grade II, or Grade III. For immunohistochemical evaluation, representative formalin-fixed, paraffin-embedded tumor blocks were selected. Sections of approximately 4µm were prepared and mounted on adhesive-coated slides. Following deparaffinization, rehydration, antigen retrieval, and blocking of endogenous peroxidase activity, tissue sections were incubated with a primary antibody against HER2/neu (rabbit polyclonal, dilution 1:250; Dako). Appropriate positive and negative controls were included with each staining batch. HER2/neu membranous staining was evaluated microscopically and categorized according to the scoring criteria used in the study as negative, weakly positive, or strongly positive. Data were entered and analyzed using SPSS (V 26.0). Categorical variables were summarized as frequencies and percentages, while age was expressed as mean ± standard deviation and range. Associations between HER2/neu expression and selected clinicopathological variables, including age, history of estrogen exposure, and histopathological grade, were assessed. A p-value of <0.05 was considered statistically significant. Ethical approval was obtained from the ethics committee of the institution before commencement of the study.

RESULTS

The study population had a mean age of 48.33 ± 10.81 years, with most patients aged 40–49 years (38.5%). Females were predominant (98.1%), indicating a higher representation of middle-aged and female patients with Guillain–Barré syndrome in this cohort (*Table I*).

Table I: Demographic characteristics of patients with invasive ductal carcinoma of breast (*n*=52)

Variables	n	%
Age group (years)		
20–39	9	17.3
40–49	20	38.5
50–59	13	25
≥60	10	19.2
Mean ± SD	48.33 ± 10.81	
Sex		
Male	1	1.9
Female	51	98.1

Grade II invasive ductal carcinoma was the most common histopathological grade, accounting for 75.0% of cases. Grade III tumors represented 21.2%, whereas only 3.8% were Grade I (*Table II*).

Table II Histopathological grade of invasive ductal carcinoma

Tumor grade	n	%
Grade I	2	3.8
Grade II	39	75
Grade III	11	21.2
Total	52	100

ISSN: 2663-9491 e-ISSN: 2789-6897

Table III shows strong HER2/neu immunohistochemical expression in 48.1% of cases, while 30.8% showed weak the studied tumors. positivity and 21.2% were negative. Thus, strong HER2/neu expression was the most frequent staining pattern among

Table III: Immunohistochemical expression of HER2/neu in invasive ductal carcinoma

HER2/neu expression	n	%
Negative	11	21.2
Weakly positive	16	30.8
Strongly positive	25	48.1
Total	52	100

Table IV shows no statistically significant association between HER2/neu expression and age (p=0.843), history of estrogen exposure (p=0.116), or histopathological tumor grade (p=0.161). However, among strongly HER2/neu-positive tumors, 80.0% were Grade II, indicating that strong expression was most frequently observed in moderately differentiated tumors.

Table IV: Association of HER2/neu expression with selected clinicopathological characteristics

Variables	Negative (n=11)	Weakly positive (n=16)	Strongly positive (n=25)	p value
	n (%)	n (%)	n (%)	
Age				
≤50 years	8 (72.7)	10 (62.5)	16 (64.0)	0.843
>50 years	3 (27.3)	6 (37.5)	9 (36.0)	
Estrogen exposure				
No	5 (45.5)	8 (50.0)	19 (76.0)	0.116
Yes	6 (54.5)	8 (50.0)	6 (24.0)	
Tumor grade				
Grade I	0 (0.0)	2 (12.5)	0 (0.0)	0.161
Grade II	7 (63.6)	12 (75.0)	20 (80.0)	
Grade III	4 (36.4)	2 (12.5)	5 (20.0)	

DISCUSSION

In the present study, the mean age of patients with invasive ductal carcinoma was 48.33 ± 10.81 years, and 65.4% were aged ≤50 years. This relatively young age distribution is consistent with reports from several Asian and African populations. In Saudi Arabia, Al-Thoubaity reported a mean age of 49 years, while the Lao study reported a mean age of 49 years [13,14]. Similarly, the Sudanese-Eritrean series reported a mean age of 48.8 years, with approximately two-thirds of patients aged ≤50 years [15]. In contrast, the Ethiopian multicenter study reported a somewhat younger mean age of 43.9 years [16]. Such differences may reflect demographic structure, genetic susceptibility, reproductive patterns, referral characteristics, and differences in breast cancer screening and early detection between populations. Regarding histological grade, 75.0% of tumors in the present study were Grade II, followed by Grade III (21.2%) and Grade I (3.8%). A similar predominance of intermediate-grade disease was observed in Côte d'Ivoire, where 56.0% of tumors were Grade II [17]. More recently, a prospective study of invasive breast carcinoma reported Grade II tumors in 79.5% of cases [18]. Conversely, poorly differentiated tumors represented 65.8% of breast cancers in the Lao series [14]. These differences may arise from variations in stage at presentation, grading reproducibility, tumor biology, and population-specific patterns of healthcare access. Nevertheless, the predominance of Grade II tumors in the present study indicates that most cancers had intermediate histological differentiation. Most notably, 48.1% of tumors showed strong HER2/neu immunohistochemical expression, while 30.8% were weakly positive and 21.2% were negative. This strong-positive proportion is considerably higher than many published series. HER2 positivity was reported in 29.0% of Sudanese and Eritrean women 15.6% in Côte d'Ivoire 8.5% in an Iranian series and approximately 17.1% when HER2-positive categories were combined in the Lao study [14,15,17,19]. In Saudi Arabia, HER2-positive tumors accounted for 11.5% of molecular subtypes [13]. Meanwhile, the Ethiopian multicenter investigation identified a HER2-enriched phenotype in 14.1% while a recent prospective invasive carcinoma study found HER2 positivity in 30.1% [16, 18]. Several factors may explain the comparatively high HER2 expression observed here. The relatively small sample of 52 cases may increase sampling variability, while referral-based recruitment can enrich the sample with biologically aggressive tumors. Differences in antibodies, fixation, antigen retrieval, interpretation thresholds, and laboratory quality assurance can also affect IHC results. Importantly, current HER2 assessment distinguishes IHC 3+ as positive, IHC 2+ as equivocal requiring in-situ hybridization, and IHC 0/1+ as negative for conventional HER2 amplification classification. Sajitha et al. reported an overall IHC-FISH concordance of 79.41%, but concordance among equivocal cases was only 14.3% [20]. Similarly, in 369 IHC 2+ invasive ductal carcinomas, Ayatollahi et al. found HER2 amplification in only 27.4% [21]. In another Indian cohort of 502 equivocal cases, FISH-based reclassification altered HER2 interpretation under updated criteria [11]. These findings emphasize that weak or equivocal IHC staining should not automatically be considered true HER2 positivity. The present study found no significant association between HER2/neu expression and age (p=0.843). This contrasts with evidence indicating more aggressive HER2-associated phenotypes among younger women. Al-Thoubaity found HER2-positive tumors more common among women younger than 50 years while Ayatollahi et al. reported HER2 amplification as associated with younger age [13, 21]. Conversely, variation in associations across studies suggests that age alone may not reliably predict HER2 status. A recent Indonesian study also demonstrated complex relationships between younger age,

breast density, HER2 expression, and aggressive molecular phenotypes [22]. Similarly, the study found no significant relationship between HER2 expression and tumor grade (p=0.161), although 80.0% of strongly positive cases were Grade II. In contrast, Mohanty found significant associations between HER2 and clinicopathological prognostic parameters while Ethiopian data linked HER2 positivity with more aggressive tumor characteristics [16,23]. Recent molecular work has further demonstrated that HER2-related signaling interacts with other pathways involved in tumor progression [24]. Such discrepancies may primarily reflect limited statistical power in the present sample, as only 52 tumors were evaluated. Clinically, the high frequency of strong HER2/neu expression has important therapeutic implications because accurately confirmed HER2-positive tumors may benefit from HER2-directed treatment. Recent evidence also demonstrates associations between HER2 amplification, higher grade, larger tumors, nodal involvement, and poorer survival whereas other biomarker studies continue to support HER2 as an integral component of breast cancer risk stratification [21,25,26]. Therefore, standardized IHC interpretation, appropriate confirmatory testing of equivocal cases, and rigorous laboratory quality control are essential to avoid both undertreatment and unnecessary HER2-targeted therapy.

LIMITATIONS

The study was limited by its small sample size and single-center design, which may restrict the generalizability of the findings. In addition, the absence of long-term follow-up and survival data limited the assessment of the prognostic significance of HER2/neu expression. Confirmatory molecular testing for equivocal HER2 cases was also not available, which may have affected the accuracy of HER2 classification.

CONCLUSION

The study demonstrated that invasive ductal carcinoma of the breast occurred predominantly in middle-aged women, with Grade II tumors being the most frequent histopathological type. Nearly half of cases showed strong HER2/neu immunohistochemical expression, indicating a substantial proportion of potentially HER2-driven tumors. However, HER2/neu expression was not significantly associated with age, estrogen exposure, or tumor grade. Accurate HER2 assessment remains clinically important for appropriate prognostic evaluation and targeted therapy selection.

RECOMMENDATIONS

HER2/neu testing should be performed routinely in patients with invasive ductal carcinoma to support prognosis and selection of HER2-targeted therapy. Ensure standardized immunohistochemical procedures and confirmatory testing for equivocal cases. Larger multicenter studies with broader clinicopathological variables and survival follow-up are recommended to clarify the relationship between HER2/neu expression and tumor behavior.

FUNDING

No funding sources

CONFLICT OF INTEREST

None declared

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

REFERENCES

1. *Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2024 May;74(3):229-63.*
2. *Lima SM, Kehm RD, Terry MB. Global breast cancer incidence and mortality trends by region, age-groups, and fertility patterns. EClinicalMedicine. 2021 Aug 1;38.*
3. *Yu AY, Thomas SM, DiLalla GD, Greenup RA, Hwang ES, Hyslop T, Menendez CS, Plichta JK, Tolnitch LA, Fayanju OM. Disease characteristics and mortality among Asian women with breast cancer. Cancer. 2022 Mar 1;128(5):1024-37.*
4. *Alam NE, Islam MS, Ullah H, Molla MT, Shifat SK, Akter S, Aktar S, Khatun MM, Ali MR, Sen TC, Chowdhury K. Evaluation of knowledge, awareness and attitudes towards breast cancer risk factors and early detection among females in Bangladesh: A hospital based cross-sectional study. PLoS One. 2021 Sep 13;16(9):e0257271.*
5. *Islam D, Islam MS. Association of hypertension, hyperlipidemia, obesity, and demographic risk factors with breast cancer in Bangladeshi women. Medicine. 2022 Nov 18;101(46):e31698.*
6. *Kumar RV, Panwar D, Amirtham U, Premalata CS, Gopal C, Narayana SM, Okaly GV, Lakshmaiah KC, Krishnamurthy S. Estrogen receptor, progesterone receptor, and human epidermal growth factor receptor-2 status in breast cancer: a retrospective study of 5436 women from a regional cancer center in South India. South Asian journal of cancer. 2018 Jan;7(01):07-10.*
7. *Hashmi AA, Mahboob R, Khan SM, Irfan M, Nisar M, Iftikhar N, Siddiqui M, Faridi N, Khan A, Edhi MM. Clinical and prognostic profile of Her2neu positive (non-luminal) intrinsic breast cancer subtype: comparison with Her2neu positive luminal breast cancers. BMC Research Notes. 2018 Aug 13;11(1):574.*
8. *Atallah NM, Toss MS, Green AR, Mongan NP, Ball G, Rakha EA. Refining the definition of HER2-low class in invasive breast cancer. Histopathology. 2022 Dec;81(6):770-85.*
9. *Swain SM, Shastry M, Hamilton E. Targeting HER2-positive breast cancer: advances and future directions. Nature reviews Drug discovery. 2023 Feb;22(2):101-26.*
10. *Pegram M, Jackisch C, Johnston SR. Estrogen/HER2 receptor crosstalk in breast cancer: combination therapies to improve outcomes for patients with hormone receptor-positive/HER2-positive breast cancer. NPJ Breast Cancer. 2023 May 31;9(1):45.*
11. *Nagarjun BR, Parikh B, Patel MN, Trivedi PJ, Patel DM. Indian data on HER2 fluorescence in situ hybridization in invasive breast cancer with immunohistochemically equivocal results as per 2018 ASCO/CAP guidelines. South Asian Journal of Cancer. 2022 Oct;11(04):281-6.*
12. *Suryavanshi M, Jaipuria J, Mehta A, Kumar D, Panigrahi MK, Verma H, Saifi M, Sharma S, Tandon S, Doval DC, Das BC. Droplet digital polymerase chain reaction offers an improvisation over conventional immunohistochemistry and fluorescent in situ hybridization for ascertaining Her2 status of breast cancer. South Asian Journal of Cancer. 2019 Oct;8(04):203-10.*
13. *Al-Thoubaity FK. Molecular classification of breast cancer: A retrospective cohort study. Annals of medicine and surgery. 2020 Jan 1;49:44-8.*
14. *Luangxay T, Virachith S, Hando K, Vilayvong S, Xaysomphet P, Arounlangsy P, Phongsavan K, Mieno MN, Honma N, Kitagawa M, Sawabe M. Subtypes of breast cancer in Lao PDR: a study in a limited-resource setting. Asian Pacific Journal of Cancer Prevention: APJCP. 2019;20(2):589.*
15. *Sengal AT, Haj-Mukhtar NS, Elhaj AM, Bedri S, Kantelhardt EJ, Mohamedani AA. Immunohistochemistry defined subtypes of breast cancer in 678 Sudanese and Eritrean women; hospitals based case series. BMC cancer. 2017 Dec 1;17(1):804.*
16. *Belachew EB, Desta AF, Gebremariam TY, Deneke DB, Ashenafi S, Yeshi MM, Fenta BD, Alem AT, Alemu A, Abafogi AK, Desta T. Immunohistochemistry-derived subtypes of breast cancer distribution in four regions of Ethiopia. Frontiers in Endocrinology. 2023 Nov 9;14:1250189.*
17. *Effi AB, Koui BS, Koffi KD, Traore ZC, Kouyate M. Breast cancer*

molecular subtypes defined by ER/PR and HER2 status: association with clinicopathologic parameters in Ivorian patients. Asian Pacific Journal of Cancer Prevention. 2016 Apr 1;17(4):1973-8.

18. *Ramasamy J, Moorthi V, Kaliyamoorthy S, Radhakrishnan V. Clinicopathological and Immunohistochemical Correlation of Stromal CD10 Expression in Invasive Breast Carcinoma: A Prospective Observational Study. Iranian Journal of Pathology. 2026 Aug 1;21(4):543.*
19. *Shandiz FH, Shabahang H, Afzaljavan F, Sharifi N, Tavasoli A, Afzalaghaee M, Roshanzamir E, Pasdar A. Ki67 frequency in breast cancers without axillary lymph node involvement and its relation with disease-free survival. Asian Pacific Journal of Cancer Prevention. 2016 Mar 1;17(3):1347-50.*
20. *Sajitha K, Arumugam M, Shetty J, Shetty RA, Asani R, Shetty PD. Breast carcinoma–A comparative study of immunohistochemistry and fluorescence in situ hybridization for Her-2 assessment and association of ER, PR, HER-2 and Ki-67 expression with clinico-pathological parameters. Iranian Journal of Pathology. 2022 Sep 2;17(4):435.*
21. *Ayatollahi H, Jafarian AH, Moghadam ZP, Ayatollahi Y, Hassankhani GG, Mehrad-Majd H. Clinicopathological Characteristics of Breast Cancer Patients with Equivocal Immunohistochemistry: A Prevalence-Based Statistical Analysis. Iranian Journal of Pathology. 2025 Jul 1;20(3):273.*
22. *Hikmawati S, Kardinah, Putri RI, Laiman V, Mupangat I, Irfan RM, Noor ZA, Laskarsantri PN, Safitri LS, Wahyono A, Heriyanto DS. High Mammographic Density in Younger Women and Its Implications for Breast Cancer Subtypes. International Journal of Breast Cancer. 2026;2026(1):8401844.*
23. *Mohanty SS. Correlation of expression of hormone and HER2 receptors with various clinico-pathological prognostic parameters and with each other in malignant breast lesion. Annals of Diagnostic Pathology. 2021 Feb 1;50:151659.*
24. *Gupta R, Gopalsamy IK, Nadukkandy AS, Singh A, Tangella CR, Alexander LE, Nair RA, Cordani M, Kumar LD. GCNT3 and ST3GAL1 expression correlates with HER2 status and MUC1/β-catenin/Cyclin D1 axis in breast cancer. BMC cancer. 2026 Mar 19;26(1):537.*
25. *Soman PS, Hemalatha A, Sreeramulu PN. Expression of BRCA1 by immunohistochemistry and its association with ER, PR, Her2neu status in infiltrative ductal carcinoma of breast. Journal of Cancer Research and Therapeutics. 2023 Jan 1;19(Suppl 2):S706-11.*
26. *Salih MM, Higgo AA, Khalifa AS, Eed EM. Incidence of Epstein-Barr Virus Among Women With Breast Cancer Using Monoclonal Antibodies for Latent Membrane Protein 1 (LMP1). in vivo. 2022;36(3):1513-8.*